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Differential expression of NFkB and response to oxidative stress in normal human melanocytes and metastatic melanoma cells.

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The transcription factor NFκB is activated by a variety of stimuli including inflammatory cytokines and reactive oxygen species (ROS). The dimeric complexes of NFκB belong to the Rel family. Two of these complexes, p65 (NFκB1) and p50 (c-Rel), are inversely expressed in normal human melanocytes (NHM) and metastatic melanoma (MM) as determined by Northern analysis. The basal DNA binding activity of NFκB in MM was 5 fold that in NHM. NFκB is constitutively active in MM probably as a consequence of the transformed phenotype. Cells were treated with free (F) or enzyme-generated (GO, glucose/gluconate oxidase) hydrogen peroxide. Butylamine (BSO) was used to inhibit the production of glutathione (GSH), an endogenous antioxidant. The expression of p65 in MM decreased 30% and 70% following GO and F, respectively and decreased 89% following BSO treatment. DNA binding activity of NFκB in MM increased 5 fold after F or GO treatment and 20 fold after BSO treatment. NHM were not affected by any treatment. GSH, being unavailable to the cell following BSO treatment, led to increased endogenous ROS further increasing NFκB activity in MM. The differential responses of NFκB in NHM and MM may serve as a useful target for preventive and therapeutic interventions.